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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,138	12/13/2001	Thomas Schultz	ORT-1548	2788

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/022,138	SCHULTZ ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Non-Final Office Action

Claims 1, 6 and 7 are pending. No claim is allowed at this time. Amendments are entered.

Summary of this Office Action dated August 17, 2008

1. Information Disclosure Statement
2. Copending Applications
3. Specification
4. 35 USC § 103(a) Rejection
5. Response to Arguments
6. Conclusion
7. Communication

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Invention

Claim 1 is drawn to an oral steroid hormone product having improved dissolution and release rate properties, said product comprising norgestimate in admixture with lactose, wherein substantially all of said norgestimate is in non-crystalline form and wherein said lactose stabilizes said norgestimate in its non- crystalline form.

Claim Rejections - 35 USC § 103 (a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6 and 7 are rejected under 35 U.S.C. 103(a) over GAST[1], in view of MORITA, MERCK[2]; JAIN et al. (European J. of Pharmaceuticals and Biopharmaceutics, 46, (1998), 177, 182); RIALKER et al and BOUCKTON et al. ((IDS references).In specification Example 1 on page 15 and Table 7 on page 21 a progestin norgestimate is disclosed.

GAST teaches a hormonal product with an excipient in crystalline and non-crystalline form, which embraces applicant's claimed invention. See the entire documents especially examples 1 and 2, claims, lines 11-19 and lines 31-67 in col. 7 of GAST.

MORITA teaches that lactose has been widely used for solid pharmaceutical preparations and many grades are available for example official grade, crystalline, anhydrous, spray dried,

or granulated lactose. Anhydrous and spray-dried and granulated lactose preparations have been used in direct compression applications. This classification is based on the manufacturing methods. On the other hand lactose has four crystallographic forms, namely alpha-monohydrate, alpha-anhydrate, beta-anhydrate and amorphous form. See the entire document especially abstract, Tables I-III and page 4076 of the reference.

MERCK in section 3751 teaches that estrone *can be* crystallized.

JAIN teaches the stability of a hydrophobic drug in presence of hydrous and anhydrous lactose. See the entire document especially abstract and introduction.

SEBHATU et al.; RIALKAR et al and BOUCKTON et al. and JAIN et al. teach the use of lactose. See the entire documents.

Instant claims differ from GAST in claiming a broader scope of non-crystalline steroid hormone. The difference between the instant invention and GAST is that the instant invention specifically claims the non-crystalline form while GAST is silent on specifically naming crystallization (Even though GAST discloses "Preferred salts of estrone include but are not limited to the sodium and piperate salt," it does not specifically use the words *crystalline* or *non-crystalline*) and MORITA et al which teaches the use of lactose in pharmaceutical preparations. MERCK in cited section 3751, teaches that estrone *can be* crystallized which means that it was ***not*** crystalline before. Also it can be used as estrones or its salts which can be crystallized or non-crystallized. GAST teaches the use of **lactose** in the formulation see example 1 on page 13 (example 1).

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[1] United States of America Patent No. 5,858,405.
[2] Merck Index, 12th edition, page 632 (3751)

It would have been obvious to one skilled in the art to prepare additional beneficial compositions for hormone replace therapy and other estrogen deficiencies because GAST teaches the limitations of the instantly claimed invention. Since GAST is silent on crystallization and lactose, the Examiner has cited MORITA which teaches use of lactose in pharmaceutical preparations and MERCK, which teaches the crystallization process of estrone to show that estrone exists in both non-crystalline and crystalline forms. JAIN teaches the use stability of hydrophobic drugs in presence of hydrous and anhydrous lactose.

Since no unexpected results and/or criticality seen, it would have been *prima facie* obvious to make and/or use non-crystalline form of the norgestimate teaching of GAST, MORITA, *MERCK, et al., RAILKAR et al, BOUCKTON et al and JAIN et al. at the time of invention presently claimed invention would have been obvious to one skilled in the art.*

The instant invention is *prima facie* obvious over the ***combined*** teachings of the prior art cited above.

See KSR Supreme Court of United States Decision KSR INTERNATIONAL CO. v. TELEFLEX INC. et al. No. 04-1350; 550 U.S.-, 82 USPQ 2d 1385 (2007) where it states that (1) "However, the issue is not whether a person skilled in the art had the motivation to combine the electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach the electronic control to the support bracket of pedal assembly". (2) "the results of ordinary innovation are not the subject of exclusive rights under the patent laws". In the present case the product as claimed would have been obvious to one skilled in the art at the time the invention was made.

In absence of any criticality and/or unexpected results instant invention is considered *prima facie* obvious to one skilled in the art.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Claims 1, 6 and 7 are rejected under 35 U.S.C. 103(a) over de HAAN, PIETER (EP 0503,521 A1) and MERCK. Both the reference teaches the formation of a tablet containing steroid specially progesterone and estrogen and excipient lactose which embraces Applicant's claimed invention.

EP '521 teaches dry pharmaceutical preparations containing ultra-low doses of one or more micronized steroidal medicinal agents in combination with a primary excipient having a high binding affinity and low demixing potential for the steroidal medicinal agent. Such excipient include spray-dried polyalcohols, granulated a-lactose monohydrate (**essentially 100 % latose**), and mixture thereof. A steroidal medicinal agent is one having a chemical structure containing a **cyclopentanoperhydrophenanthrene** backbone. The reference further teaches the formation of a tablet containing steroid specially **progesterone** and estrogen and more particularly progestetogens include 3-ketodesogesterel, (etonogestrel), desogestral, levo-norgestrel, norgerstrel, gestodene, and other compounds with similar progestogenic activity. See the entire document especially abstract, lines 16-50, page 3; lines 27-59, page 4; lines 48-58, page 5; lines 1-19, page 6; examples and claims..

MERCK in section 3751 teaches that estrone *can be* crystallized.

It would have been obvious to one skilled in the art at the time the invention was filed to prepare additional beneficial compositions as oral steroid hormone product comprising norgestimate in admixture with lactose because the reference teach the advantages of the use of lactose with a steroidal medicinal agent is one having a chemical structure containing a **cyclopentanoperhydrophenanthrene** backbone. The reference further teaches the formation of a tablet containing steroid specially **progesterone.** Norgestimate is progesterone. The motivation has been provided by the prior art to prepare such a composition. Further the term comprising in present claims allows other ingredients may be added.

The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., >*Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) ("The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps.");< *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

Since no unexpected results and/or criticality seen, it would have been *prima facie* obvious to make the compositions containing norgestimate for the reasons cited above.

See KSR Supreme Court decision KSR INTERNATIONAL CO. v. TELEFLEX INC. et al. No. 04-1350; 550 U.S.-, 82 USPQ 2d 1385 (2007) where it states that (1) "However, the issue is not whether a person skilled in the art had the motivation to combine the electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach the electronic control to the support bracket of pedal assembly". (2) "the results of ordinary innovation are not the subject of exclusive rights under the patent laws". In the present case the product as claimed would have been obvious to one skilled in the art at the time the invention was made.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Response to Arguments

Applicant argues that Merck reference fails to teach or suggest a hormonal product which includes the steroid hormone norgestimate, wherein norgestimate is in non-crystalline form. Examiner respectfully disagrees because the question should be that whether or not one skilled in the art would be able to use the teaching of the reference. In this case the reference cited by the examiner teach and suggest that steroids exist in non crystalline form. Since norgestimate is an steroid it is reasonable to expect the same. Furthermore, the reference does not have to teach every single steroid and naming them. See KSR decision.

Obviousness rejection is maintained because arguments are not found persuasive regarding the energy arguments. The crystalline form always has low energy that the non-crystalline form. A liquid form is definitely more soluble that a non crystalline form or crystalline form. This is not an invention. The question is that whether or not the basis of "argued" solubility would have been obvious to one skilled in the art at the time the invention was made. The Examiner believes that the data presented and arguments are not persuasive and are not patentable in view of the prior art on record. Applicant argue that "in the manufacture of steroid hormone products it would be highly desirable to increase the dissolution rate of the hormone while at the same time either improving or at least not reducing the physical/chemical stability of the hormone. These objectives are achieved by the claimed invention, as shown by the data set forth in Tables 1-4. In particular, the data in Table 1 demonstrate the difference in dissolution rates for non-crystalline norgestimate as compared to the lower-energy crystalline form. Note, that the dissolution rate for amorphous norgestimate at 60 minutes is about the same as the lower energy crystalline form at 120 minutes and that the dissolution rate for the amorphous form at 120 minutes is significantly higher than the rate for the crystalline form at 140 minutes. The data in Tables 2 and 3 illustrates

the effect on dissolution rate as norgestimate begins to re-crystallize from the higher energy amorphous form. As shown by these data, the dissolution rate of norgestimate decreases as the steroid converts to the lower energy crystalline form. The data in Table 4 show that the dissolution properties of norgestimate are not only dependent on storage conditions, but also on the mixing energetics imparted during the manufacturing process. Note that as energy is imparted over time and higher levels of amorphous norgestimate are present, the dissolution characteristics improve even when storage is unprotected under accelerated conditions.

As stated in the specification at page 13, lines 11-22, taken together the data from these studies demonstrate that when a mixture of an excipient and a steroid active ingredient is subjected to sufficient mechanical energy, the excipient and the steroid active ingredient form a less crystalline, more highly energetic composition. Furthermore, under appropriate mixing conditions, the lactose component stabilizes the steroid in a highly energetic, substantially non-crystalline state, thus preventing recrystallization of the steroid. The highly energetic, non-crystalline steroid active ingredient dissolves more readily and is better able to maintain desirable dissolution characteristics under a variety of conditions of ambient humidity and ambient temperature".

In specification Example 1 on page 15 and Table 7 on page 21 a progestin norgestimate is disclosed.

Since MERCK, which teaches the crystallization process of estrone to show that estrone exists in both non-crystalline and crystalline forms.

In summary Examiner concludes that claims and specification does not provide any new concept or invention for the reasons cited above. To emphasize this point Examiner would like to refer to Applicants to Genetech, 108 F.3d at 1366 and Brenner 383 U.S. 519, 536, 148 USPQ 689, 696 (1966)" which states that **"a patent is not a hunting license. It is not a reward for research, but a compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable."**

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is (571) 272-0622. The examiner can normally be reached on any business day except Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sabiha Qazi/
Primary Examiner, Art Unit 1612